

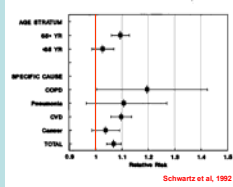
Particulate Matter and Human Health: Using Human Studies to Understand Susceptibility

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Background

Epidemiology studies have identified older people and individuals with cardiovascular disease and/or diabetes as particularly sensitive to PM



• In Philadelphia, the relative risk of mortality was found to be elevated in individuals over 65 and in those with cardiovascular disease.

• Risk of mortality was also associated with increases in total suspended particles (per 100ug/m³) :

65+ → 10% increase

Cardiovascular disease → 10% increase

	PM ₁₀	CVD	95% CI
Chicago			
With diabetes	2.01	1.40	2.62
Without diabetes	0.94	0.61	1.28
By age group			
With diabetes			
< 75	1.89	1.10	2.86
75+	2.03	1.10	2.96
Without diabetes			
< 75	0.69	0.71	1.18
75+	1.23	0.82	1.68

Zanobetti et al., 2001

• In Chicago, diabetics were found to have a 2-fold increase in risk for hospitalization for cardiovascular disease (CVD) as PM₁₀ increased (per 10ug/m³).

• Stratifying by age group (< or > 75) demonstrated that individuals over 75 and diabetic experienced the greatest risk for hospitalization for CVD with increasing PM₁₀ concentrations.

Epidemiology studies are used to identify susceptible populations, characterize risk, and are critical to understanding the health effects of PM exposure in large populations; however, they can not establish causality nor can they identify mechanisms of effect.

SCIENTIFIC QUESTION

Can human studies be used to verify the epidemiology data?

- Two types of human studies can help to more specifically identify the specific impact of PM exposure on human health:

Controlled Exposure Studies utilizing concentrated ambient particles (CAPS) allow scientists to control the dose of PM and/or co-pollutants to which study participants are exposed. These studies can be used to identify biomarkers of susceptibility and response and are powerful tools in determining cause and effect, but for ethical reasons the most sensitive groups can not be studied.

Panel Studies of individuals in "real world" environment allow scientists to determine effects in conditions which people are likely to encounter. These studies allow the scientist to observe even the most sensitive populations for cause and effect relationships between exposure and health effects. Panels of individuals are often stratified on the basis of a biomarker or genotype identified in epidemiology or controlled exposure studies.

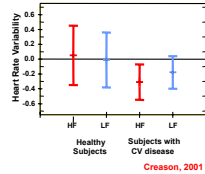
- Both approaches allow scientists to more directly identify the health effects and causative features of PM by allowing for the study of specific health endpoints, testing of specific interventions, and a detailed analysis of the particles to which individuals are exposed.

Baltimore Panel Study: PM causes changes in heart rate variability in older people with cardiovascular disease

- 26 Residents of a retirement village (average age = 81 years) with and without CV disease.
- Participants with CV disease had a decrease in heart rate variability (HRV) compared to participants without disease at ambient PM concentrations.



- Decreases in HRV have been linked to adverse outcomes, including death, in medical studies of CV disease.
- This panel study provides a potential explanation for the mortality and hospitalization findings in the epidemiology studies and demonstrate that older people with CV disease are at greater risk, but...



Do the risks to healthy older people also increase if PM concentrations increase?

Panel Studies and Controlled Exposure Studies are used to validate the data from epidemiology studies

North Carolina Diabetic Panel Study

- 22 study participants aged 40-80 with Type 2 diabetes were followed for 5 consecutive days, participants wore personal monitors that allowed for the measurement of air pollutants.
- Measures of HRV and other health endpoints were taken to identify potential mechanisms by which PM exerts its effects.
- Genomic analysis will also be performed to attempt to identify biomarkers of susceptibility.
- Study recruitment has been completed and the results are forthcoming.

An understanding of the effects of air pollutants on people with disease is important; however, is it also possible to identify people who may be at risk before they develop overt disease so that they can take suitable actions protect themselves?

These two studies provide plausibility to the previous epidemiology studies identifying the aged and people with CV disease as susceptible, but can the same be said for diabetics?

North Carolina Study of Metabolic Syndrome

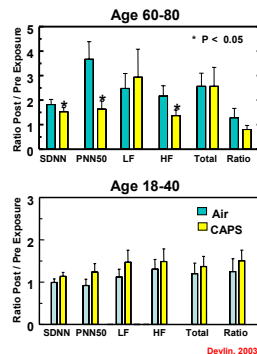
- In this study we are exposing people with metabolic syndrome to CAPS in a controlled exposure setting (recruitment is on-going).
- Metabolic syndrome is characterized by elevated blood pressure; high cholesterol, triglycerides, and blood sugar; and these individuals are typically overweight. Most people with metabolic syndrome develop CV disease or diabetes later in life.
- We will focus on various health endpoints and genomic analysis to identify biomarkers of exposure and susceptibility.
- Establishing the mechanism of effect may also provide information for future studies that might investigate behavioral, dietary, or pharmacological interventions that could protect susceptible individuals from the harmful health effects of PM.



Chapel Hill Exposure Studies:

Healthy older individuals exposed to fine CAPS experienced decreased heart rate variability while younger individuals showed no effect

- Study participants aged 60-80 and 18-40 were exposed to clean air or concentrated fine particles (PM_{2.5}).
- Average particle concentrations were 66 ug/m³ in the older cohort and 120 ug/m³ in the younger cohort.
- Study participants underwent measures of HRV before and 1 hour after exposure.
- Despite being exposed to lower PM concentrations, compared to clean air, CAPS exposure resulted in significant decreases in several HRV parameters in the older study participants while the younger participants showed no effect.
- This controlled exposure study supports the previous epidemiology studies that suggest even healthy older people may be at risk to suffer adverse health effects during episodes of high PM concentrations.



SUMMARY

- Air pollution health and exposure research has significant benefits and impacts:
 - Indicates that the current standards are necessary to protect public health.
 - Strengthens confidence in the scientific basis for these standards.
 - Provides information to inform people, particularly at-risk populations, of the harmful effects of air pollutants and to educate them to minimize exposure to air pollutants.
- A comprehensive research strategy, such as that presented here, consisting of epidemiology, panel, and controlled exposure studies is necessary to provide the greatest benefit to the public.



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